



DECLARATION OF YASUMICHI HITOSHI UNDER 37 C.F.R. §1.131	Application Number	09/843,159
	Confirmation Number	8575
	Filing Date	April 25, 2001
	First Named Inventor	Ying Luo
	Examiner	Manjunath Rao
	Group Art	1652
	Attorney Docket No.	RIGL-010CIP2

This Declaration with the attached Exhibits are being submitted in conjunction with the Applicants' Response to the Office Action dated May 26, 2004.

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I, Yasumich Hitoshi, M.D. Ph.D., do hereby declare as follows.

1. I am currently a program director at Rigel Pharmaceuticals, Inc. (hereinafter "Rigel"), and the work described in the above-referenced patent application was performed with my knowledge.
2. I understand that the claimed subject matter of the above-referenced patent application relates to assays for identifying agents that modulate the poly(A) ribose polymerase activity of Tankyrase H.
3. I have been asked to provide factual evidence relating to the activities of Rigel and Rigel's patent counsel with respect to the claimed subject matter, prior to October 25, 1999 (the filing date of the above-referenced patent application).

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4. I have reviewed the Exhibits attached hereto and they all relate to the activities of Rigel or Rigel's patent counsel with respect the claimed subject matter, prior to October 25, 1999.
5. Prior to June 11, 1999, the inventors of the above-referenced patent application identified the sequence of the ADP-ribose polymerase domain of Tankyrase H and identified that Tankyrase H had poly(A) ribose polymerase activity. Evidence for this is provided in Exhibit A. All redacted dates are prior to June 11, 1999.
6. Further, between June 11, 1999, and July 21 1999, the inventors worked towards identifying the full length sequence of Tankyrase H for use in the above-referenced screening assays. Evidence for this is provided in Exhibits B and C. The dates have not been redacted in these exhibits.
7. Finally, between July 20, 1999 and October 25, 1999, the above-referenced patent application was drafted at the law firm of Flehr, Hobach, Test, Albritton and Herbert (hereinafter "Flehr"), the law firm contracted to draft the above-referenced patent application. Evidence for this is provided in Exhibits D – H. The dates have not been redacted in these exhibits.
8. Exhibit A consists of a print-out of Tankyrase H amino acid and nucleic acid sequences. On pages, 2, 6 and 7 of this Exhibit, Tankyrase H is identified as having a poly(A) ribose polymerase domain. The date of the print-out was prior to June 11, 1999.
9. Exhibit B consists of a presentation that was made by Xiang Xu, an inventor, that identifies Tankyrase H as having poly(A) ribose polymerase activity on page 3. The date of this presentation was June 15, 1999.
10. Exhibit C consists of signed laboratory notebook pages from Simon Yu, a colleague at Rigel Pharmaceuticals, Inc. These notebook pages show results of experiments directed towards identifying the full length sequence of Tankyrase H for use in the above-


referenced screening assays. The notebook pages are dated July 9, July 13, July 15, July 16 and July 21, 1999, respectively.

11. Exhibit D consists of a letter from Nicole Verona of Rigel to Ms. Robin Silva of Flehr), the law firm contracted to draft the above-referenced patent application. The letter references an invention disclosure (i.e., eight packages of information) for use in preparation of the above-referenced patent application. The date of the letter is July 20, 1999.
12. Exhibit E consists of a letter from Nicole Verona of Rigel to Ms. Robin Silva of Flehr. The letter references diskettes for use in preparation of the above-referenced patent application. The date of the letter is July 22, 1999.
13. Exhibit F consists of a file information page from Flehr, indicating that the file for the above-referenced patent application was opened on July 26, 2003.
14. Exhibit G consists of an e-mail dated August 30, 1999, from Nicole Verona of Rigel to Ms. Dolly Vance of Flehr regarding questions about the above referenced invention disclosure. The body of this e-mail contains text of previous e-mails dated August 20, 1999 and August 26, 1999, also relating to the above referenced invention disclosure.
15. Exhibit H consists of a letter from Nicole Verona of Rigel to Ms. Dolly Vance regarding further documents for use in drafting the above-referenced patent application. The date of the letter is September 30, 1999.
16. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18

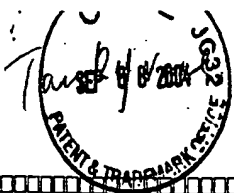
of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: 9/3/04


Yasumichi Hitoshi, M.D. Ph.D.,

Attachments: Exhibits A - G



final Exhibit A 09/843,159
in xxu (common) Seqn fold from 1.1

Longest ORF frame 1 of 1060 amino acids
From amino acid position 84 to 1143

1 MVQTPMLEIIGIILLSMKLQKERLMFALCCYFAVLLQHGAEPTILNTDGR TALDLADPS
61 AKAVLTGEYKKDELLESARGNEEKMMALLTPLNVNCHASDGRKSTPLHLAAGYNRVKIV
121 QLLLQHGADVHAKDGLVPLHNACSYGHYEVTELLVKHGACVNAMDWLQFTPLHEAASK
181 NRVEVCSLLLSYGADPTLLNCHNKSALDLAPTQPKERLAYEFKGHSLLQAAREADVTRI
241 KHLHLEMVNFKHPQTHETALHCAAASPYPKRKQICELLRLKGANINEKTKEFLTPLHVA
301 SEKAHNDVVEVVVKEAKVNALDNLGQTSLHRAAYCGLQTCRLLLSYGCDPNIISLQGF
361 TALQMGNNVQQLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQS
421 TPLHFAAGYNRVSVVEYLLQHGADVHAKDKGLVPLHNACSYGHYEAELLVKHGA VNV
481 ADLWKFTPLHEAAAKGYEICKLLLQHGADPTKKNRDGNTPLDLVKDGDTDIHYLLRGDA
541 ALLDAAKKGCLARVKLLSSPDNVNCRDTQGRHSTPLHLAAGYNNLEVAEYLLQHGADVNA
601 QDKGGLIPLHNAASYGHVDAALLIKYNACVNATDKWAFTPLHEAAQKGR TQCALLLAH
661 GADPTLKNQEGQTPLDLVSADDSALLTAAMPSPALPSCYKQVNLGVRS PGATADALSS
721 GPSSPSSLSAASSLDNLSGSFSELSLVSSSGTEGASSLEKKEVPGVDF SITQFVRNLGL
781 EHLMDIFEREQITLDVLVEMGHKELKEIGINAYGHRHKLKIGVERLISGQOGLNPYLTIN
841 TSGSGTILIDLSPDDEKFQSVVEEMQSTVREHRDGGHAGGIFNRYNLIKIQVCNKKLWE
901 RYTHRRKEVSEENHNHANERMLFHGSPFVNAIHKGFDERHAYIGGMFGAGIYFAENSSK
961 SNQVYVYGGGGTGCGPVHKDRSCYICHRQLLFCRVTLGKSFLOFSAMKMAHSPGHHSVTG
1021 RPSVNGLALA EYVIYRGEQAYPEYLITYQIMRPEGMVDGZ

1 GAAGTGCAGCGGGGTGGATTTCTCGGAATTGCCTTAGTAGTAGTACCACCCAAGGCACTG
61 CTTAGGTACCAGTCTGCTTAGTGAGAGTCCCTCTGGCTTTATCATTAAAGGTTTGGGC
121 GGAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAATGTCCAAGCACGTGATGATG
181 GGGGCCTTATCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCC
241 TTTTGCGACATGGTGACAGACCCAATGCTCGAGATAATTGGAATTATACCTCTCTCCATG
301 AAGCTGCAATTAAGGAAAGATTGATGTTTGCATTGTGTGCTATTTTGCAGTGCTGTTA
361 CAGCATGGAGCTGAGCCAACCATCTAAATACAGATGGAAGGACAGCATTGGATTTAGCA
421 GATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAGATGAACCTTAGAAAGT
481 GCCAGGAGTGGCAATGAAGAAAAATGATGGCTCTACTCACACCATTAATGTCAACTGC
541 CACGCAAGTATGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTA
601 AAGATTGTACAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGAT
661 CTGGTACCATTACACAATGCCTGTTCTTATGGTCAATTATGAAGTAAC TGAACCTTTGGTC
721 AAGCATGGTGCCTGTGTAATGCAATGGACTTGTGGCAATCACTCCTCTTCATGAGGCA
781 GCTTCTAAGAACAGGGTTGAAGTATGTTCTCTTCTTAAAGTTATGGTGCAGACCCAACA
841 CTGCTCAATTGTACAATAAAGTGCTATAGACTTGGCTCCACACCACAGTTAAAGAA
901 AGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTT
961 ACTCGAATCAAAAACATCTCTCTCGGAAATGGTGAATTTCAAGCATCTCAAACACAT
1021 GAAACAGCATTGCATTGTGCTGCTGCATCTCCATATCCCAAAGAAAGCAAATATGTGAA
1081 CTGTTGCTAAGAAAAGGAGCAAAACATCAATGAAAAGACTAAAGAATCTTGACTCCTCTG
1141 CACGTGGCATCTGAGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAAACATGAAGCA
1201 AAGGTTAATGCTCTGGATAATCTTGGTCAGACTTCTCTACACAGAGCTGCATATTGTGGT
1261 CATCTACAAACCTGCCGCTACTCCTGAGCTATGGGTGTGATCCTAACATTATATCCCTT
1321 CAGGGCTTTACTGCTTTACAGAGTGGGAAATGAAAATGTACAGCAACTCCTCCAAGAGGGT
1381 ATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGAT
1441 GTCGAAACTGTAAAAAACTGTGTACTGTTTCAAGAGTGCTCAACTGCAGAGACATTGAAGGG
1501 CGTCAGTCTACACCACCTTCAATTTTGCAGCTGGGTATAACAGAGTGTCCTGGTGGATAT
1561 CTGCTACAGCATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCCTGTACCTTTGCAC
1621 AATGCATGTTCTTATGGACATTATGAAGTTGCAGAACTTCTTGTAAACATGGAGCAGTA
1681 GTTAATGTAGCTGATTTATGGAAATTTACACCTTTACATGAAGCAGCAGCAAAAGGAAAA
1741 TATGAAATTTGCAAACTTCTGCTCCAGCATGGTGACAGCCCTACCAAAAAAACAGGGAT
1801 GGAAATACTCTTTGGATCTTGTAAAGATGGAGATACAGATATTCAATTATCTGCTTAGG
1861 GGAGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGAAGAAGTTG
1921 TCTTCTCTGATAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACAT

1981 TTAGCAGCTGGTTATAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGAT
2041 GTGAATGCCCAAGACAAAGGAGGACTTATTCTTTACATAATGCAGCATCTTACGGGCAT
2101 GTAGATGTAGCAGCTCTACTAATAAAGTATAATGCATGTGTCAATGCCACGGACAAATGG
2161 GCTTTCACACCTTTGACGAAGCAGCCCAAAAGGGACGAACACAGCTTTGTGCTTTGTTG
2221 CTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGGAAGGACAAACACCTTTAGATTTA
2281 GTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCCATCTGCTCTGCCC
2341 TCTTGTACAGCCTCAAGTGCTCAATGGTGTGAGAAGCCAGGAGCCACTGCAGATGCT
2401 CTCCTTCAGGTCCATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACCTTA
2461 TCTGGGAGTTTTTCAGAACTGTCTTCATTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCC
2521 AGTTTGGAGAAAAAGGAGGTTCCAGGAGTAGATTTTAGCATAACTCAATTCGTAAGGAAT
2581 CTTGGACTTGAGCCTAATGGATATATTTGAGAGAGAACAGATCACTTTGGATGTATTA
2641 GTTGAGATGGGACACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGGACATAGGCAC
2701 AAATAATTAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGTCTTAACCCATATTTA
2761 ACTTTGAACACCTCTGGTAGTGGACAATTCTTATAGATCTGTCTCCTGATGATAAGAG
2821 TTTCACTCTGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTCAT
2881 GCAGGTGGAATCTTCAACAGATACAATATTCTCAAGATTCAGAAGGTTTGTAAACAAGAAA
2941 CTATGGGAAAGATACACTCACCAGGAGAAAAGAAGTTTCTGAAGAAAACCACAACCATGCC
3001 AATGAACGAATGCTATTTTCATGGGTCTCCTTTTGTGAATGCAATTATCCACAAAGGCTTT
3061 GATGAAAGGCATGCGTACATAGGTGGTATGTTTGGAGCTGGCATTATTTTGTGAAAAC
3121 TCTTCCAAAAGCAATCAATATGTATATGGAATTGGAGGAGGTACTGGGTGTCCAGTTCAC
3181 AAAGACAGATCTTGTACATTGTCCACAGGCAGCTGCTCTTTTGGCGGTAACCTTGGGA
3241 AAGTCTTTCTGCAGTTCAGTGCAATGAAAATGGCACATTCTCTCCAGGTCACTACTCA
3301 GTCAGTGGTAGGCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGA
3361 GAACAGGCTTATCCTGAGTATTTAATTACTTACCAGATTATGAGGCTGAAGGTATGGTC
3421 GATGGATAAATAGTTATTTAAGAACTAATTCCTACTGAACCTAAATCATCAAAGCAGC
3481 AGTGGCCTCTACGTTTTACTCCTTTGCTGAAAAAAAAAAAA

ref|NP_003738.1|PTNKS| TANKYRASE >gi|3929219 (AF082556) TRF1-interacting
ankyrin-related

ADP-ribose polymerase [Homo sapiens] Length = 1327
Score = 1640 bits (4199), Expect = 0.0
Identities = 790/1023 (77%), Positives = 871/1023 (84%), Gaps = 11/1023 (1%)
Query: 35 VLLQHGAEPTILNTDGRALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLN 94
VLLQHGAA+P I NTDG++ALDLADPSAKAVLTGEYKKDELLE+ARSGNEEK+MALLTPLN
Sbjct: 300 VLLQHGADPNIRNTDGKSALDLADPSAKAVLTGEYKKDELLEAARSGNEEKLMMALLTPLN 359
Query: 95 VNCHASDGRKSTPLHLAAGYNRVKIVQLLQHGADVHAKDKGDLVPLHNACSYGHYEVE 154
VNCHASDGRKSTPLHLAAGYNRV+IVQLLQHGADVHAKDKG LVPLHNACSYGHYEVE
Sbjct: 360 VNCHASDGRKSTPLHLAAGYNRVRIVQLLQHGADVHAKDKGGLVPLHNACSYGHYEVE 419
Query: 155 LLVKHGACVNAMDLWQFTPLHEAASKNRVEVCSLLSYGADPTLLNCHNKSALDLAPTQ 214
LL+KHGACVNAMDLWQFTPLHEAASKNRVEVCSLLS+GADPTL+NCH KSA+D+APTQ+
Sbjct: 420 LLLKHGACVNAMDLWQFTPLHEAASKNRVEVCSLLSHGADPTLVNCHGKSAVDMAPTPE 479
Query: 215 LKERLAYEFKGHSLQAAAREADVTRIKKHLSEMVNFKHPQTHETALHCAAASPYPKRKQ 274
L+ERL YEFKGHSLQAAAREAD+ ++KK L+LE++NFK PQ+HETALHCA AS +PKRKQ
Sbjct: 480 LRERLTYEFKGHSLQAAAREADLAKVKKTLALEIINFKQPQSHETALHCAVASLHPKRKQ 539
Query: 275 ICELLLRKGANINEKTKEFLTPLHVASXXXXXXXXXXXXXXXXXXXXLDNLGQTSLHRAA 334
+ ELLLRKGAN+NEK K+F+TPLHVA+ LD LGQT+LHRAA
Sbjct: 540 VTELLLRKGANVNEKNKDFMTPLHVAAERAHNDVMEVLHKHGAKMNALDTLGQTLHRAA 599
Query: 335 YCGLQTCRLLLSYGCDPNIIISLQGFALQMGNEENVQQLLEGISLGNSEADRQLLEAAK 394
GHLQTCRLLLSYG DP+IISLQGFAL QMGNE VQQ+L E + S+ D +LLEA+K
Sbjct: 600 LAGHLQTCRLLLSYGSDPSIIISLQGFALQMGNEAVQQILSESTPIRTSDVDYRLLEASK 659

Query: 395 AGD VETVKLC TVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQH GADVHAKDKGGLV 454
 AGD+ETVK+LC+ Q+VNCRD+EGR STPLHFAAGYNRVSVVEYLL HGADVHAKDKGGLV
 Sbjct: 660 AGDLETVKQLCSSQNVNCRDLEGRHSTPLHFAAGYNRVSVVEYLLHHGADVHAKDKGGLV 719

Query: 455 PLHNACSYGHYEVAELLVKHGAVNVADLWKFTPLHEAAAGKGYEICKLLLQH GADPTKK 514
 PLHNACSYGHYEVAELLV+HGA VNVADLWKFTPLHEAAAGKGYEICKLLL+HGADPTKK
 Sbjct: 720 PLHNACSYGHYEVAELLVRHGASVNVADLWKFTPLHEAAAGKGYEICKLLLKH GADPTKK 779

Query: 515 NRDGNTPLDLVKDGD TD IHYXXXXXXXXXXXXXXXXXXXXXRVKLS SPDNVNCRDTQGRHST 574
 NRDGNTPLDLVK+GD TD RV+KL +P+N+NCRDTQGR+ST
 Sbjct: 780 NRDGNTPLDLVKEGD TD IQDLLKGDAALLDAAKKGCLARVQKLC TPENINCRDTQGRNST 839

Query: 575 PLHLAAGYNNLEVAEYLLQH GADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNAT 634
 PLHLAAGYNNLEVAEYLL+HGADVNAQDKGGLIPLHNAASYGHVD+AALLIKYN CVNAT
 Sbjct: 840 PLHLAAGYNNLEVAEYLLLEHGADVNAQDKGGLIPLHNAASYGHVDIAALLIKYNTCVNAT 899

Query: 635 DKWAF TPLHEAAQKGR TQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPPS 694
 DKWAF TPLHEAAQKGR TQLCALLLAHGADPT+KNQEGQTPLDL +ADD+ ALL AMP
 Sbjct: 900 DKWAF TPLHEAAQKGR TQLCALLLAHGADPTMKNQEGQTPLDLATADDIRALLIDAMPPE 959

Query: 695 ALPSCYKPQ---VLNGVRS PGATXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX 751
 ALP+C+KPQ V + SP +T
 Sbjct: 960 ALPTCFKPQATVVSASLISPAST-----PSCLSAASSIDNLTGPLAELAVGGASNAG 1011

Query: 752 XXXXXXXXXXXXKEVPGVDFSITQFVRNLGLEHLMDIFEREQITLDVLVEMGHKELKEIGIN 811
 + EV G+D +I+QF+++LGLEHL DIFE EQITLDVL +MGH+ELKEIGIN
 Sbjct: 1012 DGAAGTERKEGEVAGLDMNISQFLKSLGLEHLRDIFETEQITLDVLADMGHEELKEIGIN 1071

Query: 812 AYGHRHKLIKVERLISGQQGLNPYLT LNTSGSGTILIDLSPDDKEFQSVEEEMQSTVRE 871
 AYGHRHKLIKVERL+ GQQG NPYLT + GTIL+DL+P+DKE+QSVEEEMQST+RE
 Sbjct: 1072 AYGHRHKLIKVERLLGGQGTNPYLT FHCNVNQTILLDLAPEDKEYQSVEEEMQSTIRE 1131

Query: 872 HRDGGHAGGIFNRYN ILKIQKVCNKKLWERYTHRRKEVSEENHNHANERMLFHGSPFFVNA 931
 HRDGG+AGGIFNRYN+++IQKV NKKL ER+ HR+KEVSEENHNH NERMLFHGSPFF+NA
 Sbjct: 1132 HRDGGNAGGIFNRYN VIRIQKVVNKKLRERFCHRQKEVSEENHNHNHNERMLFHGSPFFINA 1191

Query: 932 IIHKG FDERHAYIGGMFGAGIYFAENSSKSNQVYVYGIGGGTGCPVHKDRSCYICHRQLLF 991
 IIHKG FDERHAYIGGMFGAGIYFAENSSKSNQVYVYGIGGGTGCP HKDRSCYICHRQ+LF
 Sbjct: 1192 IIHKG FDERHAYIGGMFGAGIYFAENSSKSNQVYVYGIGGGTGCP THKDRSCYICHRQMLF 1251

Query: 992 CRVTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIM 1051
 CRVTLGKSFLQFS MKMAH+PPGHHSV GRPSVNGLA AEYVIYRGEQAYPEYLITYQIM
 Sbjct: 1252 CRVTLGKSFLQFSTMKMAHAPPGHHSVIGRPSVNGLAYAEYVIYRGEQAYPEYLITYQIM 1311

Query: 1052 RPE 1054
 +PE
 Sbjct: 1312 KPE 1314

 GAAGTGCAGCGGGGTGGATTTCCTGGAATTGCCTTAGTAGTAGTACCACCAAGGCACTG
 CTTAGGTACCACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTTATCATTAAAGGTTTTGGG
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 GGGGGCCTTATTCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTC
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 TACAGCATGGAGCTGAGCCAACC
 ATCTTAAATACAGATGGAAGGACAGCATTGGATTAGCAGATCCATCT

121 GCCAAAGCAGTGCCTTACTGGTGAATATAAGAAAGATGAACTCTTAGAAAGTGCCAGGAGT
 181 GGCAATGAAGAAAAATGATGGCTCTACTCACACCATTAAATGTCAACTGCCACGCAAGT
 241 GATGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAAAGATTGTA
 301 CAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCA
 361 TTACACAATGCCTGTTCTTATGGTCATTATGAAGTAACTGAACCTTTTGGTCAAGCATGGT
 421 GCCTGTGTAATGCAATGGACTTGTGGCAATTCACCTCTTCATGAGGCAGCTTCTAAG
 481 AACAGGGTTGAAGTATGTTCTCTTCTTAAAGTTATGGTGCAGACCCAACTGCTCAAT
 541 TGTCACAATAAAGTGCTATAGACTTGGCTCCACACCACAGTTAAAGAAAGATTAGCA
 601 TATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTTACTCGAATC
 661 AAAAAACATCTCTCTGGAATGCTGCAATTTCAAGCATCCTCAAACACATGAAACAGCA
 721 TTGCATTGTGCTGCTGCATCTCCATATCCAAAAGAAAGCAAAATATGTGAAGTGTGCTA
 781 AGAAAAGGAGCAAAACATCAATGAAAAGACTAAAGAATTCTTGACTCCTGTCACGTGGCA
 841 TCTGAGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAACATGAAGCAAAGGTTAAT
 901 GCTCTGGATAATCTTGGTCAGACTTCTCTACACAGAGCTGCATATTGTGGTCATCTACAA
 961 ACCTGCCGCTACTCCTGAGCTATGGGTGTGATCCTAACATTATATCCCTTCAGGGCTTT
 1021 ACTGCTTTACAGATGGGAAATGAAAATGTACAGCAACTCCTCAAGAGGGTATCTCATT
 1081 GGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGATGTCGAACT
 1141 GTAAAAAACTGTGTACTGTTTCAAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCT
 1201 ACACCCTTCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGAATATCTGTACAG
 1261 CATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCTTGTACCTTTGCACAATGCATGT
 1321 TCTTATGGACATTATGAAGTTGCAGAACTTCTTGTAAACATGGAGCAGTAGTTAATGTA
 1381 GCTGATTTATGGAATTTACACCTTTACATGAAGCAGCAGCAAAAGGAAAATATGAAATT
 1441 TGCAAACTTCTGCTCCAGCATGGTGCAGACCCCTACCAAAAAAACAGGGATGGAATACT
 1501 CCTTTGGATCTTGTAAAGATGGAGATACAGATATTCATTATCTGCTTAGGGGAGATGCA
 1561 GCTTTGCTAGATCTGCCAAGAAGGGTTGTTAGCCAGAGTGAAGAAGTTGTCTTCTCCT
 1621 GATAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATTTAGCAGCT
 1681 GGTATAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCC
 1741 CAAGACAAAGGAGGACTTATTCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTA
 1801 GCAGCTCTACTAATAAGTATAATGCATGTGTCAATGCCACGGACAAATGGGCTTTCACA
 1861 CCTTTGCACGAAGCAGCCCAAAAGGGACGAACACAGCTTTGTGCTTTGTGCTAGCCCAT
 1921 GGAGCTGACCCGACTCTTAAAAATCAGGAAGGACAAACACCTTTAGATTAGTTTCAGCG
 1981 GATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCCATCTGCTCTGCCCTCTTGTAC
 2041 AAGCCTCAAGTGCTCAATGGTGTGAGAAGCCAGGAGCCACTGCAGATGCTCTCTCTCA
 2101 GGTCCATCTAGCCCATCAAGCCTTTCTGACCCAGCAGTCTTGACAACCTTATCTGGGAGT
 2161 TTTTCAGAACTGTCTTCATTAGTTAGTTCAAGTGGAACAGAGGGTCTTCCAGTTTGGAG
 2221 AAAAGGAGGTTCCAGGAGTAGATTTTAGCATAACTCAATTCTGTAAGGAATCTTGGACTT
 2281 GAGCCTAATGGATATATTGAGAGAGAACAGATCACTTTGGATGTATTAGTTGAGATG
 2341 GGGCACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGGACATAGGCACAACTAATT
 2401 AAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGTCTTAACCCATATTTAACTTTGAAC
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 AACAGATACAATATTCTCAAGATTCAGAAGGTTTGTAAACAGAACTATGGGA
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 CAGGCTTATCCTGAGTATTTAATTACTTACCAGATTATGAGGCTGAAGGTATGGTCG
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1 GGCACGAGCTGCAACGAAATGGAAAGATTGATGTTTTGCATTGTGTTACAGCATGGA
 61 GCTGAGCCAACCR10ATCCTAAATACAGATGGAAGGACAGCATTGGR9ATTTAGCAGATCCATCT
 121 GCCAAAGCAGTGR8CTTACTGGTGAATATAAGAAAGATGAACTCTTAGAAAGTGCCAGGAGT

181 GGCAATGAAGAAAAATGATGGCTCTACTCACACCATTAAATGTCAACTGCCACGCAAGT
241 GATGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAAAGATTGTA
301 CAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCA
361 TTACACAATGCCCTGTTCTTATGGTCATTATGAAGTAACTGAACCTTTGGTCAAGCATGGT
421 GCCTGTGTAAATGCAATGGACTTGTGGCAATCACTCCTCTTCATGAGGCAGCTTCTAAG
481 AACAGGGTTGAAGTATGTTCTCTCTCTTAAAGTTATGGTGCAGACCCAACACTGCTCAAT
541 TGTACAATAAAAGTGTCTATAGACTTGGCTCCACACCACAGTTAAAGAAAGATTAGCA
601 TATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTTACTCGAATC
661 AAAAAACATCTCTCTGGAATGGTGAATTTCAAGCATCCTCAAACACATGAAACAGCA
721 TTGCATTGTGCTGCTGCATCTCCATATCCAAAAGAAAGCAAATATGTGAAGTGTGCTA
781 AGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCA
841 TCTGAGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAACATGAAGCAAAGGTTAAT
901 GCTCTGGATAATCTTGGTCAGACTTCTCTACACAGAGCTGCATATTGTGGTCATCTACAA
961 ACCTGCCGCCTACTCCTGAGCTATGGGTGTGATCCTAACATTATATCCCTTCAGGGCTTT
1021 ACTGCTTTACAGATGGGAAATGAAAATGTACAGCAACTCCTCCAAGAGGGTATCTCATT
1081 GGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAAGGGCTGGAGATGTCGAAACT
1141 GTAAAAAACTGTGTACTGTTTACAGAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCT
1201 ACACCACTTCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGGAAATATCTGCTACAG
1261 CATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCCTTGACCTTTGCACAATGCATGT
1321 TCTTATGGACATTATGAAGTTGCAGAACTTCTGTGTTAAACATGGAGCAGTAGTTAATGTA
1381 GCTGATTTATGGAATTTACACCTTTACATGAAGCAGCAGCAAAAGGAAAATATGAAATT
1441 TGCAAACTTCTCTCAGCATGGTGCAGACCCCTACCAAAAAAACAGGGATGGAAATACT
1501 CCTTTGGATCTTGTGTTAAAGATGGAGATACAGATATTCATTATCTGCTTAGGGGAGATGCA
1561 GCTTTGCTAGATGCTGCCAAGAAGGGTTGTTAGCCAGAGTGAAGAAGTTGTCTCTCCT
1621 GATAATGTAATTTGCCGCGATACCAAGGCAGACATTCAACACCTTTACATTTAGCAGCT
1681 GGTATAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCC
1741 CAAGACAAAGGAGGACTTATTCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTA
1801 GCAGCTCTACTAATAAAGTATAATGCATGTGTCAATGCCACGGACAAATGGGCTTTCACA
1861 CCTTTGCACGAAGCAGCCCAAAAGGGACGAACACAGCTTTGTGCTTTGTTGCTAGCCCAT
1921 GGAGCTGACCCGACTCTTAAAAATCAGGAAGGACAAACACCTTTAGATTTAGTTTCAGCG
1981 GATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCCATCTGCTCTGCCCTCTTGTTAC
2041 AAGCCTCAAGTGCTCAATGGTGTGAGAAGCCCAGGAGCCACTGCAGATGCTCTCTCTTCA
2101 GGTCCATCTAGCCCATCAAGCCTTTCTGACGCCAGCAGCTTGCACAACCTTATCTGGGAGT
2161 TTTTCAGAACTGTCTTCAATAGTTAGTTCAAGTGGAAACAGAGGGTGCCTCCAGTTTGGAG
2221 AAAAAAGGAGGTTCCAGGAGTAGATTTTAGCATAACTCAATTGTAAGGAATCTTGGACTT
2281 GAGCACCTAATGGATATATTTGAGAGAGAACAGATCACTTTGGATGTATTAGTTGAGATG
2341 GGGCACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGGACATAGGCACAACTAATT
2401 AAAGGAGTCGAGAGACTTATCTCCGACAACAAGGTCTTAACCCATATTTAATTGAAC
2461 ACCTCTGGTAGTGAACAATTTATAGF5ATCTGTCTCCTGATGATAAAGAGTTTCAGTCTF6
2521 GTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGAF7TGGAGGTCATGCAGGTGGA
2581 ATCTTCAACAGATACAATATTTCTCAAGATTGAGAAGGTTTGTAAACA
Plus
3'end

GTCTCCTGATGATAAAGAGTTTCAGTCTGTGGAGGAAGAGATGCAAAGT
ACAGTTCGAGAGCACAGAGATGGAGGTCATGCAGGTGGAATCTTC
AACAGATACAATATTTCAAGATTCAGAAGGTTTGTAACAAGAACTATGGGA
AAGATACACTCACCGGAGAAAAGGTTTCTGAAGAAAACCACAACCATGCCAATGA
ACGAATGCTATTTTCATGGGTCTCCTTTTGTGAATGCAATTATCCACAAAGGCTTTGATG
AAAGGCATGCGTACATAGGTGGTATGTTTGGAGCTGGCATTTATTTGCTGAAAACCTTT
CCAAAAGCAATCAATATGTATATGGAATTGGAGGAGGTACTGGGTGTCCAGTTACAAAAG
ACAGATCTTGTACATTTGCCACAGGCAGCTGCTCTTTTGGCGGTAACCTTGGGAAAG
TCTTTCTGCAAGTTCAGTGAATGAAAATGGCACATTCTCTCCAGGTCATCACTCAGTC
ACTGGTAGGCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAGAA
CAGGCTTATCTGAGTATTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCG
ATGGATAAATAGTTATTTAAGAACTAATCCACTGAACCTAAAATCATCAAAGCAGC
AGTGGCCTCTACGTTTACTCCTTTGCTGAAAAA

gi|3929219 (AF082556) TRF1-interacting ankyrin-related ADP-ribose polymerase
[Homo sapiens] Length = 1327

Score = 464 bits (1181), Expect = e-130

Identities = 223/309 (72%), Positives = 249/309 (80%) Frame = +2

Query: 2 LEMVNFKHPQTHETALHCAAASPYPKRKQICELLRLKGANINEKTKEFLTPLHVASXXXX 181

LE++NFK PQ+HETALHCA AS +PKRKQ+ ELLRLKGAN+NEK K+F+TPLHVA+

Sbjct: 511 LEIINFKQPQSHETALHCAVASLHPKRKQVTELLRLKGANVNEKNKDFMTPLHVAAERAH 570

Query: 182 XXXXXXXXXXXXXXXXLDNLGQTSLHRAAYCGHLQTCRLLLSYGCDPNIIISLQGFTALQM 361

LD LGQT+LHRAA GHLQTCRLLLSYG DP+IISLQGFTA QM

Sbjct: 571 NDVMEVLHKHGAKMNALDTLGQTALHRAALAGHLQTCRLLLSYGSDPSIISLQGFTAAQM 630

Query: 362 GNENVQQLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHF 541

GNE VQQ+L E + S+ D +LLEA+KAGD+ETVK+LC+ Q+VNCRD+EGR STPLHF

Sbjct: 631 GNEAVQQLSESTPIRTSDVDYRLLEASKAGDLETVKQLCSSQNVNCRDLEGRHSTPLHF 690

Query: 542 AAGYNRVSVVEYLLQHGADVHAKDKGGLVPLHNACSYGHEVAELLVKHGAVNVADLWK 721

AAGYNRVSVVEYLL HGADVHAKDKGGLVPLHNACSYGHEVAELLV+HGA VNVADLWK

Sbjct: 691 AAGYNRVSVVEYLLHHGADVHAKDKGGLVPLHNACSYGHEVAELLVRHGASVNVADLWK 750

Query: 722 FTPLHEAAAKGYEICKLLLQHGADPTKKNRDGNTPLDLVKDGDXTIQXXXXXXXXXXXXX 901

FTPLHEAAAKGYEICKLLL+HGADPTKKNRDGNTPLDLVK+GDT IQ

Sbjct: 751 FTPLHEAAAKGYEICKLLLKHGADPTKKNRDGNTPLDLVKEGDTDIQDLLKGDAALLDA 810

Query: 902 XXKGCFXQI 928

KGC ++

Sbjct: 811 AKKGCCLARV 819

Longest ORF frame 2 of 310 amino acids

From amino acid position 1 to 311

1 LEMVNFKHPQTHETALHCAAASPYPKRKQICELLRLKGANINEKTKEFLTPLHVASEKAH

61 NDVVEVVVKHEAKVNALDNLGQTSLHRAAYCGHLQTCRLLLSYGCDPNIIISLQGFTALQM

121 GNENVQQLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHF

181 AAGYNRVSVVEYLLQHGADVHAKDKGGLVPLHNACSYGHEVAELLVKHGAVNVADLWK

241 FTPLHEAAAKGYEICKLLLQHGADPTKKNRDGNTPLDLVKDGDXTIQDLLRGDAXXLD

301 AXKGCFXQIX

1 GCTGGAAATGGTGAATTTCAAGCATCTCTCAAAR7CACATGAAACAGCATTGCATTGTGCTGC

61 TGCATCTCCATATCCCAAAGAAAGCAAAR6TATGTGAACGTGTGCTAAGAAAAGGAGCAAA

121 R5CATCAATGAAAAGACTAAAGAATTCTTGACTCTCTGCACGTGGCATCTGAGAAAGCTCA

181 TAATGATGTTGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATCT

241 TGGTCAGACTTCTCTACACAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCTACT

301 CCTGAGCTATGGGTGTGATCCTAACATTATATCCCTTCAGGGCTTTACTGCTTTACAGAT

361 GGGAAATGAAAATGTACAGCAACTCTCCAAGAGGGTATCTCATTAGGTAATTCAGAGGC

421 AGACAGACAATGCTGGAAGCTGCAAAGGCTGGAGATGTGAAACTGTAAAAAACTGTG

481 TACTGTTCAAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCTACACCACCTTCATTT

541 TGCAGCTGGGTATAACAGAGTGTCCGTGGTGAATATCTGCTACAGCATGGAGCTGATGT

601 GCATGCTAAAGATAAAGGAGGCCTTGACCTTTGCACAATGCATGTTCTTATGGACATTA

661 TGAAGTTGCAGAACTTCTTGTTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAA

721 ATTTACACCTTTACATGAAGCAGCAGCAAAAGGAAAATATGAAATTTGCAAACCTTCGCT

781 CCAGCATGGTGCAGACCTTACCAAAAAAACAGGGATGGAAATACTCCTTTGGATCTTGT

841 TAAAGATGGAGATACANATATTCAAGATCTGCTTAGGGGAGATGCANNNTTNCATAGATGC

901 TGCCNANAAGGGTTGTTTTANCCAGATTNAA

>EST assembled

Good protein homology to

gi|3929221 (AF082557) TRF1-interacting ankyrin-related
ADP-ribose polymerase [Homo sapiens]
TITLE Tankyrase, a poly(ADP-ribose) polymerase at human telomeres
JOURNAL Science 282, 1484-1487 (1998)
Longest ORF frame 3 of 258 amino acids
HVASEKAHNDVVEVVVKHEAKVNALDNLGQTSLHRAAXCGHLQTCRLLLSYGCDPNIISL
QGFTALQMGNEENVQQLLEGISLGNSEADRLLEAAKAGDVETVKKLCTVQSVNCRDIEG
RQSTPLHFAAGYNRVSVVEYLLQHGADVHAKDKGGLVPLHNACSYGHYEVAELLVKHGAV
VNVADLWKFTPLHEAAAKGKYEICKLLQHGADPTKKNRDGNTPDLVKDGDXTXIQDLLR
GDAXXLDAAAXKGCFXQIX
TGCACGTGGCATCTGAGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAACATGAAG
R2CAAAGGTTAATGCTCTGGATAATCTTGGTCAGACTTCTCTACACAGAGCTGCATNTTGTG
GNCATCTACAAACCR1TGCCGCCTACTCTGAGCTATGGGTGTGATCCTAACATTATATCCC
TTCAGGGCTTTACTGCTTTACAGATGF4GGAATGAAAATGTACAGCAACTCTCCAAGAGG
GTATCTCATTAGGTAATTCAGAGGCAGACAGAR4CAATTGCTGGAAGCTGCAAAGGCTGGAG
ATGTCGAAACTGTAAAAAACTGTGTACTGTTR3CAGAGTGTCAACTGCAGAGACATTGAAG
GGCGTCAGTCTACACCACTTCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGAAT
ATCTGCTACAGCATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCCTTGACCTTTGC
ACAAATGCATGTTCTTATGGACATTATGAAGTTGCAGAACTTCTTGTAAACATGGAGCAGF3
TAGTTAATGTAGCTGATTTATGGAATTTACACCTTTACATGAAGCAGCAGCAAAAGGAA
AATATGAAATTTGCAAACTTCTGCTCCAGCATGGTGF1CAGACCCTACCAAAAAAACAGGG
ATGGAATACTCCTTTGGATCTTGTTAAAF2AGATGGAGATACANATATTCAAGATCTGCTTA
GGGAGATGCANNTTTNCTAGATGCTGCCNANAAGGGTTGTTTTANCCAGATTNAA

TGCACGTGGCATCTGAGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAACATGAAG
CAAAGGTTAATGCTCTGGATAATCTTGGTCAGACTTCTCTACACAGAGCTGCATNTTGTG
GNCATCTACAAACCTGCCGCCTACTCTGAGCTATGGGTGTGATCCTAACATTATATCCC
TTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTACAGCAACTCTCCAAGAGG
GTATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAG
ATGTCGAAACTGTAAAAAACTGTGTACTGTTCAGAGTGTCAACTGCAGAGACATTGAAG
GGCGTCAGTCTACACCACTTCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGAAT
ATCTGCTACAGCATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCCTTGACCTTTGC
ACAAATGCATGTTCTTATGGACATTATGAAGTTGCAGAACTTCTTGTAAACATGGAGCAG
TAGTTAATGTAGCTGATTTATGGAATTTACACCTTTACATGAAGCAGCAGCAAAAGGAA
AATATGAAATTTGCAAACTTCTGCTCCAGCATGGTGCAGACCCTACCAAAAAAACAGGG
ATGGAATACTCCTTTGGATCTTGTTAAAGATGGAGATACANATATTCAAGATCTGCTTA
GGGAGATGCANNTTTNCTAGATGCTGCCNANAAGGGTTGTTTTANCCAGATTNAA

>cip6clp5F2

TCATTATCTGCTTAGGGGAGATGCAGCTTT
GCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGCGAAGAAGTTGTCTTCTCCTGATAA
TGTAATTTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATTTAGCAGCTGGTTA
TAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCAAGA
CAAAGGAGGACTTATTCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGC
TCTACTAATAAAGTATAATGCATGTGTCAATGCCACGGACAAATGGGCTTTACACCTTT
GCACGAAGCAGCCCCAAAAGGGACGAACACAGCTTTGTGCTTTGTTGCTAGCCCATGGAGC
TGACCCGACTCTTAAAAATCAGGAAGGACAAACACCTTTAGATTTAGTTTCAAGCGGATGA
TGTCAGCGCTCTTCTGACAGTAGCCATGCCCATCTGCTCTGCCCTCTTGTTACAAGC
CTCAAGTGTCAATGGGTGTGAGAAGCCCAGGAGCCACTGCAGATGCTCTCTCTTCAGGT
CCATCTAGCCCATCAAGCCTTTCTGCANCCAGCAGTCTTGACAACCTATTCTGGGAGTTT

>cip6c2p5-F3

GGATGGAAATACTCCTTTGGATCTTGTTAAAGATG
GAGATACAGATATTCAAGATCTGCTTAGGGGAGATGCAGCTTTGCTAGATGCTGCCAAGA
AGGGTTGTTTAGCCAGAGTGAAGAAGTTGTCTTCTCCTGATAATGTAAATTGCCGCGATA
CCAAGGCAGACATTCAACACCTTTACATTTAGCAGCTGGTTATAATAATTTAGAAGTTG
CAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCAAGACAAAGGAGGACTTATTC
CTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTACTAATAAAGTATA



Exhibit B
09/843,159

6/15/1999

w/ Tank northam
blob
↳ This slide is for Cassen

Chk1 two-hybrid screening

Bait: Chk1

is a protein kinase required for cell cycle arrest in response to DNA damage

Hit: a novel protein homology to ATP-dependent RNA helicase
belongs to the DEAD-box RNA helicase family

The fission yeast *cdc28(+)* encodes a member of the DEAD-box family of putative RNA helicases involved in pre-mRNA splicing and cell cycle progression

a new gene encoding a putative DEAD box helicase have been isolated to suppress uncontrolled mitosis by overexpression *cdc25* in fission yeast
(Chk1 and 14-3-3 proteins also show up in this screening)

It is interesting to characterize the interaction of Chk1 and the novel RNA helicase and its role in cell cycle control

Potential targets for further pursuing

p21 hit:	Tankyrase homolog
Traf4 hit:	Cdk liked kinase
hRad9 hit:	PP5
PNCA hits:	a novel helicase a human homolog of SNM1 a novel endo/exo-ribonuclease
Chk1 hit:	an ATP-dependent RNA helicase homolog

Target validation:

- full length cloning
- examine the RNA expression in tumor verse normal tissues
- peptide binding library screening in YTH---->functional assay
- generate dominant-negative mutant

p21 hit: a Tankyrase homolog

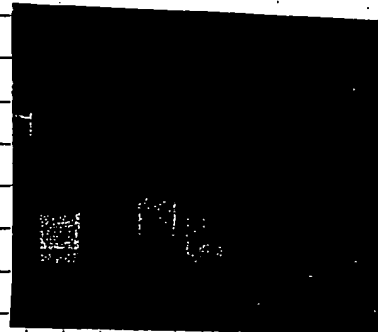
Tankyrase (a poly(ADP-ribose) polymerase at human telomeres)

- a protein with homology to ankyrin and to the catalytic domain of ADP-ribose polymerase (PARP)
- is localized to human telomeres
- binds to the telomeric protein TRF1 (telomeric repeat binding factor-1)
- is a positive regulator of telomere length maintenance

TITLE _____

From Page No. _____

Reheat 10 but use N/A/RH
 PCR primer N/A/RH N/A/RH
 templates: N/A/RH 2.1
 N/A/RH 2.2
 Cap30. 5'0 X

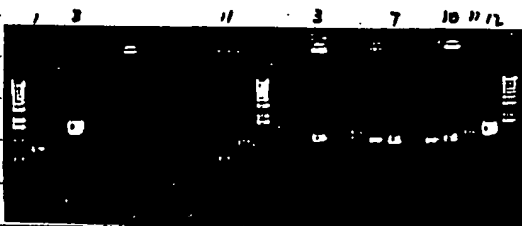


7/13/02 #2-CapA1 & #2-CapA2

PCR insert screening primer, N/A/RH

CAPS #2-CapA1

#2-CapA2



7/19/02 screening more

N/A/RH → 2-CapA1



7/14/02

mini plasmid prep

#2-CapA2: #2-CapA1
3 7 10 11 12

#2-CapA2-3 (N/A/RH)

-10
-12

#2-CapA1-3

-11

300 ng each

Result

no sequence

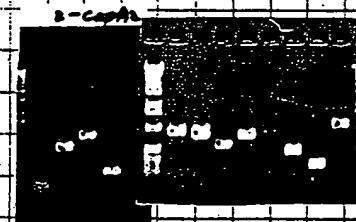
7/14/02

no sequence

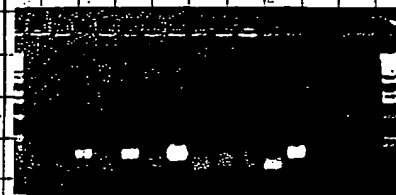
isoform 1

isoform 3

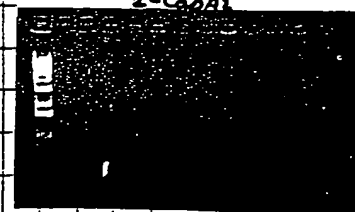
7/12



F3/RH check



2-CapA2



#1, PCR check N/A/RH

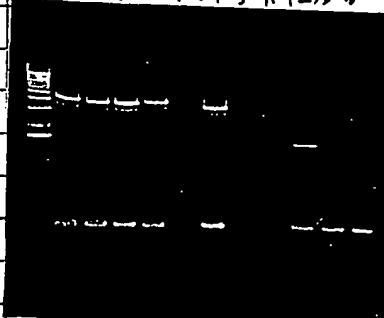
#2-CapA1-

3 7 10 11 12

#1-CapA1-

1 3 11 12

223, 224, 225



7/12

To Page No. 137

Witnessed & Understood by me,

JH

Date

8/27/99

Invented by

Sg

Recorded by

Sg

Date

7/13/99

From Page No. 155

7/1/99 5'-end cloning.

from library

Template

primer

① HB/plb

FAL/R14

② H. Leuk/plb

.

③ 42ap mix

FAS/R14

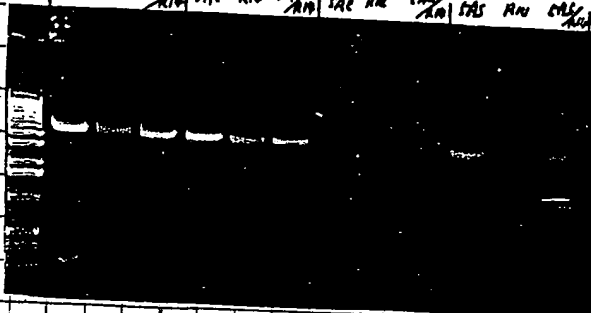
④ HB/psport

FAS/R14

Gap30 (2'40')

HB/plb H. Leuk/plb 42ap mix HB/psport

CAL R14 FAY R14 FAL R14 FAY R14 FAS R14 FAS R14 FAS R14



7/3/99

2P

F8/R11 F8/R11

#2-D1

3

4

Cap23

GP

GP

GP

GP

#2-D1 (FAL/R14)

#2-D3

#2-D4

#2-D5 (FAS/R14)

#2-D2

(FAY/R14)

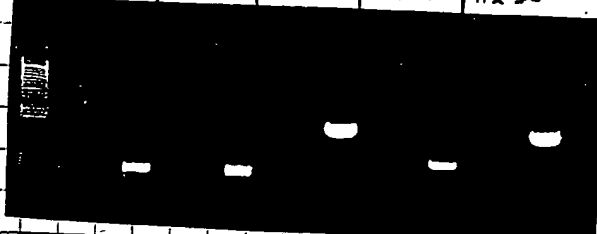
(FAS/R14)

Insert screen

2-D3, D4, D5

T/A cloning #2P

#2-D1 #2-D2 #2-D3 #2-D4 #2-D5



7/11

pck insert screening primer F8/R11

pck insert screening primer F8/R11

#2-D3

F8/R11

#2-D4

GP

GP

GP

GP

GP

#2-E1 (F8/R11)

#2-E2

#2-E3

#2-E4

#2-E5

X

(F8/R11)

(F8/R11)

F8/R11

F8/R11

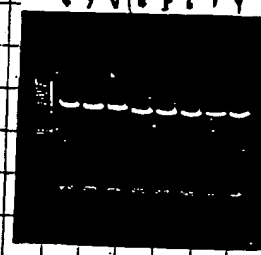
To sequence #14

T/A cloning

Check insert with F13/R11 (11)

2-D3- 2-D4-

6 7 8 9 5 6 1 9



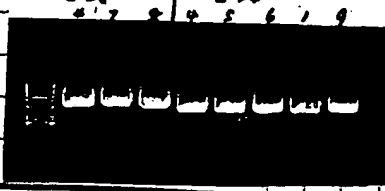
7/1-99

Mini prep

In on gel

each

Core = 300



Witnessed & Understood by me,

JH

Date

8/2/99

Invented by

Sg

Recorded by

Sg

Date

7/13/99

To Page No. _____

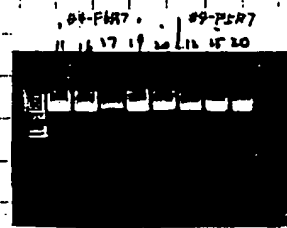
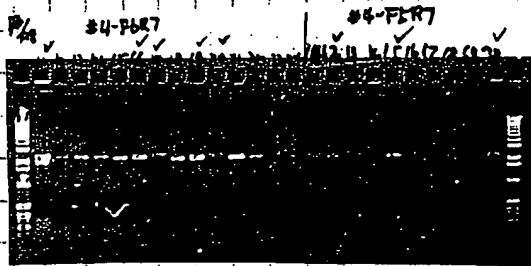
TITLE _____

PC-140 #4.

From Page No. 121

7/12/99

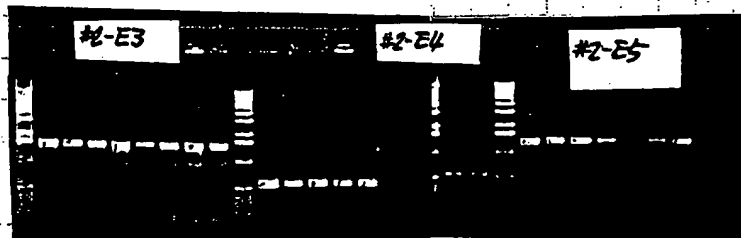
PCR insert screening again (last time the amount clones are not enough)
 primer use FS/R8



#4-F6R7-11 } 7/13
 -9 } to sequence
 -20 }
 #4-F5R7-15 }

7/15/99

Clones PCR insert screening



7/13/99 insert check result: all of them have band.

To Page No. _____

Witnessed & Understood by me,

JH

Date

8/1/99

Invented by

S1

Recorded by

S2

Date

7/13/99

From Page No. 100

7/1/99 (2)

Compare pH of PCR Buffer -

API RIL API RIL

template H₂O (Marathon) 30mg/L 1 in 25 PCR
 + 0.5 1 M HCl + 0.5 1 M HCl
 + 1.5 " + 0.5 "
 + 2.5 " + 0.5 "

Cap30

nauseous

HCl

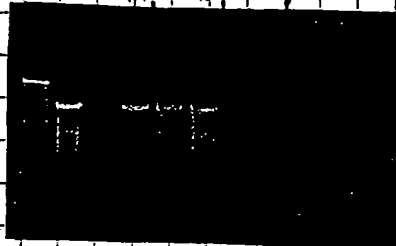
0

0.5

0.5

0.5

API RIL API RIL API RIL

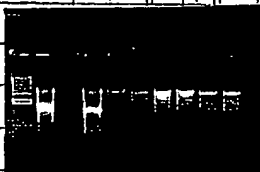


X

Try New buffer & API.

API RIL API RIL

API RIL API RIL API RIL New Buff. 10mg/L



X

To Page No. _____

Witnessed & Understood by me,

JH

Date

8/2/99

Invented by

G2

Recorded by

G2

Date

7/15/99

7/14/90 (2-5-) (page bti) (change) (sequence)

① { T+B X 6/25, p111 } { Back kit X } { #2-54-1 (449) }
 { H. leuk/pl V (R16, R11) } { clonable kit V } { -3 }
 { } { } { -4 } ✓

② { HB(R) V 6/30, p115-7 } { #2-C1-6 (113) }
 { T+B V R14 } { -7 }
 { H. Mela X } { -12 }
 { H. Liver/pl V } { -18 }
 { } { #2-C2-1 (113) }
 { } { -5 }
 { } { #2-C3-11 (113) }
 { } { -17 }
 { } { -18 }

③ { HB/pl V 7/2, p126-7 } { X HB to send 9/10 } { mini & clones }
 { H. leuk/pl V R16 } { 15 x 6 → } { but distinct p115 F3/R11 class X }
 { 4 Zap 21X - } { axes → } { no to sequencing }
 { H. B/ps V } { X to min clone plate } { give p115 9/10 F3 }
 { } { } { #2-D3 (H. leuk) }
 { } { } { #2-D4 (4 Zap unit) }
 { } { } { #2-D5 (HB/pl) }

3. [redacted]

① [redacted] myself X 7/1, p123, 128 { Normal Body }
 HB R16 { difference p115 but }
 { C. Nardus } X p115 adaptor problem

② clonable Marathon Body 2/18, 7/6, p119
 { H. Fetal Brain X }
 { H. Fetal Liver X }
 { H. Leukocyte X }

✓ 3. [redacted] 7/9, p140-5. ✓

{ HB primer T ✓ }
 { HB, V R14 X }

7/20 p117

{ #2-CapA1-3 (112) V isoform 1 }
 { -11 (112) V isoform 3 }
 { #2-CapA2-3 (112) }
 { -10 }
 { -12 (112) V no seq }
 { (p115 F3/R11 check) }
 { #2-CapA1-29 (112) V }
 { -33 (112) V }
 { -34 (112) V }
 { #2-CapA2-26 (112) V }
 { -29 (112) V }

Result: got 2 isoform from Smart RACE. & got isoform from Library method.

But Marathon did work.

7/32 finish it.

TITLE

CZPS #2

Project No. _____

Book No. _____

137

From Page No. ¹²⁵

← M/M prep 2x each

1 conc = 200 ng/μl



- F13/R11 insert check again

#2-CapA1-29

-33

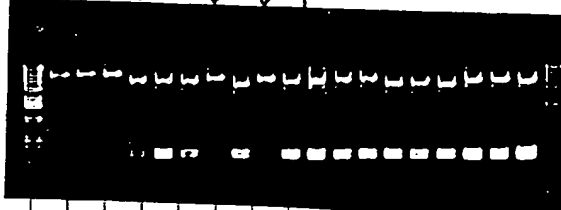
-34

to sequence 7/20 (3)

2-CapA2-26

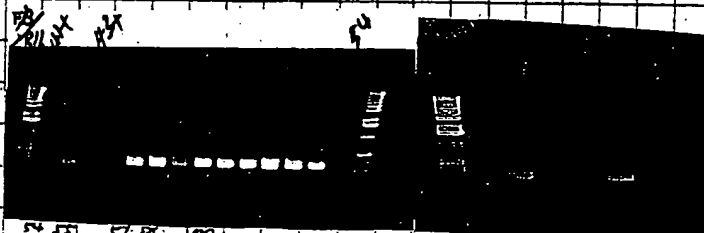
-29

2-CapA1-29
-33
-34
2-CapA2-26
-29
2-EB-1
-2
-4
2-E4-1
-3
-4
2-E5-1
-2
-3



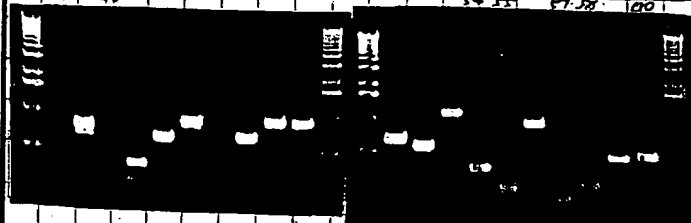
7/21 (3) pick 20 clones from #2-CapA1

PCR insert screen Nup/R11 & F13/R11



N/R11 PCR

41 43



Pathogen is primary

#2-CapA1-60

(N/R11)

#2-CapA1-60

CZPS #2-CapA1-60 to sequence (7/21)

mini (Seq-PI35)

To Page No. _____

Witnessed & Understood by me,

JH

Date

8/17/99

Invented by

SY

Recorded by

SY

Date

7/21/99



RIGEL

4938

Exhibit D 09/843,149

FLEHR, HOBACH, TEST
ALBRITTON & HERBERT

1999 JUL 22 AM 9.02

RECEIVED

July 20, 1999

RIGEL, INC.

VIA FEDERAL EXPRESS

Ms. Robin Silva
Flehr, Hobach, Test, Albritton, & Herbert
4 Embarcadero Center, Suite 3400
San Francisco, California 94111-4187

Per RMS - OPEN
AS UNITY

Re: Provisional Patent Applications.

Dear Ms. Silva,

Per Brian Cunningham's request, enclosed with this letter are eight packages of information generated by Dr. Ying Luo in preparation for provisional patent application filings. Each package pertains to a different genetic sequence that Rigel believes may be commercially useful. Each package contains relevant scientific materials, journal references and abstracts of proposed gene functions.

Please file a provisional patent application for each document.

If you have any questions, please call me at 650-624-1106.

Respectfully yours,

Nicole A. Verona
Rigel Pharmaceuticals, Inc.

Exhibit DE 09/845,141

FLEHR, HOBACH, TEST
ALBRITTON & HERBERT

1999 JUL 23 AM 10:04

RECEIVED

July 22, 1999

RIGEL

RIGEL, INC.

VIA FEDERAL EXPRESS

Ms. Robin Silva
Flehr, Hobach, Test, Albritton, & Herbert
4 Embarcadero Center, Suite 3400
San Francisco, California 94111-4187

ORIGINAL Diskette in
P-68287

Re: Provisional Patent Applications.

Dear Ms. Silva,

It was a pleasure to meet you today. I'm sorry that I did not see you leave; I had intended to give you these diskettes before the end of our meeting.

On these diskettes are the documents that we reviewed earlier. The new document that Ying gave to me today will be ready on Monday.

If you have any questions, please call me at 650-624-1106.

Respectfully yours,

Nicole Verona

Nicole A. Verona
Rigel Pharmaceuticals, Inc.

Exhibit # F 09/843,149

DOCKETING/BILLING SYSTEM FILE INFORMATION
(Patent/Design Patent)

Date: July 26, 1999

File No.: A-68292

Client: Rigel Pharmaceuticals Access Code: 4931

Client

Attorney: DJB/RMS/DAV

Ref. No.:

New ☒

Update ☐

Close ☐

Parent ☐

Div. ☐

CPA ☐

CIP ☐

Subject Description

Title: TANKYRASEH, A Cell Cycle Protein

Inventors: Ying Luo

Serial No.:

Filing Date:

Patent No.:

Issue Date:

Assignee:

Related Files:

If Foreign file, please provide corresponding U.S. Serial Number
or Patent Registration Number.

Misc. (Include any action items and due dates here!):

Submitted by: Gail Clark

Date: July 26, 1999

cc: Accounting

Docketing - Foreign

Docketing - US

2x hixt AG 09/843, 149

From: Nicole Verona <NVerona@rigel.com>
To: "'dvance@flehr-iplaw.com'" <dvance@sfpo.fhtah.fleh...
Date: 8/30/99 4:01pm
Subject: FW: FW: info

Dear Dolly,

I forwarded your questions to Ying Luo and this is the response I received from him. I hope this helps. Also, I've got copies of the TNIK manuscript figures that you need. Would you like me to fax them to you?

Nicole

-----Original Message-----

From: Ying Luo [mailto:yluo@rigel.com]
Sent: Sunday, August 29, 1999 2:44 PM
To: Nicole Verona
Subject: Re: FW: info

7868 PAN is from PCNA screening. tankyraseH is from CIP screening. CIP is also called p21. R0101 has an entry in GenBank with full length sequence with a name called KIAA0101. No functional annotation about R0101. PP5 was cloned and published before. The novelty is we can link PP5 to RAD9, a cell cycle checkpoint control protein. You should have all figures of TNIK manuscript already. TNIK nucleotide sequences are attached. PAN nucleotide sequence is already in Genbank.

Ying

At 03:21 PM 8/26/99 -0700, you wrote:

>Hi Ying!

>

>Here are some of the questions I need to discuss with you.

>

>Nicole

>

>-----Original Message-----

>From: Dolly Vance [mailto:dvance@flehr-iplaw.com]
>Sent: Friday, August 20, 1999 1:42 PM
>To: nverona@rigel.com
>Subject: info

>

>

>Dear Nicole,

>Hope you're well. Here's a complete list of what I am missing from the
>initial 9 disclosures.

>

>1) The names of binding partners (if any actual) for CAH and
>tankyraseH.

>2) The nucleic acid and amino acid sequences for PAN and TNIK
>(actually, all figures that go with the manuscript for TNIK).

>3) Please confirm that R0101 and PP5 are NOT novel, and that all
>others are novel.

>
>Thanks. Dolly

>P.S. I understand your hours are reduced. Any chance you can give me a

>time frame for providing the above information? Thanks again, Dolly

>

RIGEL

FLEHR, HOHBACH, TEST,
ALBRITTON & HERBERT

1999 OCT -1 AM 10:05

RECEIVED

Exhibit H 09/30/99 149

RIGEL, INC.

September 30, 1999

Ms. Dolly Vance
Flehr, Hohbach, Test, Albritton and Herbert LLP
4 Embarcadero Center, Suite 3400
San Francisco, California 94111-4187

Dear Dolly,

Enclosed are documents pertaining to the cell-cycle patent applications that you requested.

The documents include:

1. TankyraseH abstracts involving TRF, P21, and PARP
2. TankyraseH nucleotide sequence alignment report
3. TankyraseH amino acid sequence alignment report
4. R0101 figures with corrected CDK 2, 3, and 4 labels
5. Mkinase nucleotide and amino acid sequences with its kinase domain and nuclear localization sequence (NLS) highlighted

Additional information will be sent to you next week.

Please call or email me if you have any questions.

Sincerely,

Nicole Verona

Nicole Verona